REMARKS

A. REQUEST FOR RECONSIDERATION

Applicants have carefully considered the matters raised by the Examiner in the outstanding Office Action dated June 4, 2008, but remain of the opinion that patentable subject matter is present. Applicants respectfully request reconsideration of the Examiner's position based on the following remarks.

B. SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Further to the Supplemental Information Disclosure Statement submitted on June 27, 2007 and pursuant to M.P.E.P. §609 and 37 C.F.R. §§1.56, 1.97-1.99, Applicants herewith submit form PTO/SB/08a, which lists co-pending applications related to the subject matter claimed herein. The $180.00 fee set forth in 37 C.F.R. 1.17(p) is fee is hereby paid along with the online filing.

C. THE INVENTION

The present invention is directed to a pharmaceutical composition comprising a combination of formoterol and a steroidal anti-inflammatory agent.

One of the novel aspects of the invention is that in the claimed composition, the formoterol is in solution, the steroidal anti-inflammatory agent is in suspension and the water is propellant-free. Another novel aspect is that the concentration of formoterol in the composition is no greater than 200 μg/mL and is stable for long term storage at a concentration suitable for direct administration. These aspects are neither taught nor suggested in the prior art. Applicants therefore submit that these novel aspects of the present invention define over the references cited by the Examiner.

D. STATUS OF THE CLAIMS

Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 93 and 99-146 are presented for further prosecution. No amendments have been made herein.

E. PRIOR ART REJECTIONS

The Examiner has made the following four rejections:

(1) Claims 1, 3-21, 23-38, 40-64, 69-74, 78-83, 87-89, 99-112, 117-119 and 122-128 are unpatentable over Hochrainer et al. (U.S. 6,150,418) in view of Carling et al. (U.S. 5,674,860) and PDR;

(2) Claim 93 is unpatentable over Hochrainer in view of Carling and PDR, and further in view of PDR, pages 482, 535, 537 and 2828;

(3) Claims 113-116 and 120-121 are unpatentable over Hochrainer in view of Carling and PDR, and further in view of Hardman et al. (Goodman Gilman's *The Pharmacological Basis of Therapeutics*, 1996, page 665) or Leckie et al. (*Novel Therapy of COPD*, abstract, Jan 2000); and

(4) Claims 129-146 are unpatentable over Hochrainer in view of Remington's Pharmaceutical Sciences, Seventeenth Edition, 1985, pages 1443 and 1451.

The Examiner had cited the above-mentioned prior art references in previous Office Actions, including the Office Action dated August 27, 2007, to teach compositions containing formoterol and steroid which are suitable for long term storage and direct administration, wherein the formoterol is in solution and the steroid is in suspension. The Examiner took the position that although none of the references cited expressly teach dilute formoterol-containing compositions suitable for long term storage and direct administration, one of skill in the art would have arrived at the present invention. Applicants responded to this point made by the Examiner on February 22, 2008, by directing the Examiner's attention to commonly assigned U.S. Patent Nos. 6,667,344 (the '344 patent), 6,814,953 (the '953 patent) and commonly assigned U.S. Patent Application Serial No. 10/887,785, (now U.S. Patent No. 7,348,362 (the '362 patent)), directed to formoterol-containing compositions suitable for long term storage and direct administration and methods of treating bronchoconstrictive disorders by administering such compositions. The compounds claimed in the '344 patent, the '953 patent and the '362 patent were found by the USPTO to be patentable over Hochrainer, Carling, the PDR, Hardman and Leckie which have also been relied upon in the present application.

In an Office Action dated June 4, 2008, the Examiner maintained the above-mentioned prior art rejections, stating that an issued U.S. patent is not a legal precedent,

and that the evidence of record shows that the subject matter as claimed is a combination of known components selected for their known properties for treatment of obstructive respiratory disease and asthma. The Examiner's points are addressed below.

1. THE USPTO HAS REPEATEDLY FOUND THAT DILUTE AQUEOUS FORMULATIONS WERE PATENTABLE OVER THE REFERENCES RELIED UPON BY THE EXAMINER

With respect to the Examiner's position regarding the three issued U.S. patents covering dilute aqueous formoterol-containing compositions, Applicants specifically traverse the Examiner's position that the commonly assigned U.S. patents covering similar subject matter should not be treated consistently. The consistent treatment of applications during prosecution, and the subsequent issue of such consistent patents promotes the public notice function of patents and protects the public's reliance on definitive statements made during prosecution. *See Medinol v. Guidant*, 2004 U.S. Dist LEXIS 1905, *19 (citing *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1323 (Fed. Cir. 2003)). Moreover, the CAFC has repeatedly held that when the written descriptions of two applications are essentially identical, they should be treated consistently. *See Elkay Mfg. Co. v. EBCO Manufacturing Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999); *Jonsson v. The Stanley Works*, 903 F.2d 812, 817-818 (Fed. Cir. 1990). Thus, the presecution history in any patent that has issued applies with equal force to subsequently prosecuted applications that contain the same limitations. *See Medinol*, 2004 U.S. Dist LEXIS 1905, *19 (citing *Elkay Mfg.*, 192 F.3d at 980).

In Applicant's previous response of February 22, 2008, Applicants noted that the claimed formoterol and steroid containing compositions are substantially the same as the dilute aqueous formoterol-containing compositions which are suitable for long term storage and direct administration as claimed in the commonly assigned patents, the '344 patent, the '953 patent and the '362 patent. Additionally, the USPTO had issued Notices of Allowance for three applications, U.S. Patent Application Nos. 11/688,429, 11/688,436, and 11/688,450 (the continuation applications), which are continuation applications of the '362 patent, and are also directed to dilute aqueous formoterol-containing compositions. Thus, the USPTO has consistently, and repeatedly found that

such dilute aqueous formoterol-containing compositions as claimed in the '344 patent, the '953 patent, the '362 patent and the continuation applications are patentable over the same prior art cited by the Examiner in the present application.

Applicants note that the aforementioned patents and applications share the same assignee and share the same three inventors. Moreover, the specification of the present application is essentially identical to the specifications of the '344 patent and the '953 patent. *Elkay Mfg. Co.*, 192 F.3d at 979. A difference between the present application and the aforementioned commonly assigned patents and applications is that the present application includes subject matter directed to compositions containing formoterol and a steroidal anti-inflammatory agent suitable for long term storage and direct administration. Thus, the scope of the claims in the present application is actually narrower than the scope of the claims which issued in the aforementioned patents and applications. Thus, since the broader claims were found patentable over the prior art cited by the Examiner, the narrower claims currently pending in the present application should also be deemed patentable. Moreover, the USPTO has repeatedly and consistently found that the prior art references neither teach nor suggest the formoterol-containing compositions of the aforementioned patents and applications, therefore, the references are no more relevant to claims directed to compositions containing a combination of formoterol and steroid.

Moreover, it is important to note that the present application shares the same priority date as the '344 patent and the '953 patent. This date is more than two years earlier than the priority date of the '362 patent and the continuation applications. All share a common thread, namely, dilute formoterol-containing compositions suitable for long term storage and direct administration without dilution. The USPTO found the dilute aqueous formoterol-containing compositions as claimed in the '362 patent and the continuation applications to be patentable and the claim language relating to formoterol in the claims of the present application is consistent in scope with the claims of the '362 patent and the continuation applications. Thus, the ineluctable conclusion which must be found is that the claims pending in the present application are patentable.

Therefore, the present application, having the same assignee, the same inventors, the same or an earlier priority date, the same limitations and essentially the same disclosure should be treated consistently with the '344 patent, the '953 patent, the '362

patent, and the continuation applications. Thus, the claimed subject matter in the present application should be found patentable over the prior art. Additionally, Applicants would be amenable to submitting Terminal Disclaimers in view of commonly assigned U.S. Patent Nos. 6,667,344, 6,814,953 and 7,348,362 if that would help place the application in condition for allowance.

2. THE CLAIMS ARE NOT OBVIOUS OVER HOCHRAINER IN VIEW OF ANY COMBINATION OF REFERENCES RELIED UPON BY THE EXAMINER

Applicants submit that the present invention does not provide predictable changes over the prior art, rather, the present invention provides novel aspects that are neither taught nor suggested in the prior art. None of the prior art references teach compositions containing formoterol in solution and steroid anti-inflammatory agent in suspension. Additionally, none of the prior art references teach such compositions where the concentration of formoterol is about 5 μg/mL to about 200 μg/mL. Furthermore, none of the references teach or suggest that such dilute compositions would be stable for long term storage and direct administration.

Hochrainer does not teach compositions containing formoterol and a steroid anti-inflammatory where the formoterol is in solution and the steroid is in suspension and wherein the formoterol concentration is between 5 μg/mL and 200 μg/mL and the compositions are suitable for long term storage and administration without dilution (col. 4, lines 9-13). The Examiner has taken the position that the stability of such dilute compositions as claimed are predictable in light of the prior art cited (Page 13 of the Office Action). However, Applicants submit that the prior art cited by the Examiner teaches that the claimed compositions are not predictable, and thus, not obvious over the prior art.

Hochrainer does not teach compositions wherein the formoterol is in solution and the steroidal anti-inflammatory agent is in suspension. Indeed, Hochrainer teaches away from compositions as claimed in the present application because Hochrainer teaches that formoterol can be in solution or in suspension (Abstract). In contrast, the present application requires that the formoterol be in solution. Additionally, Hochrainer is

completely silent on whether the steroid is in solution or suspension. In contrast, the present application requires that the formoterol is in solution and the steroidal anti-inflammatory is in suspension. Moreover, Hochrainer further teaches away from the claimed subject matter of the present application in that Hochrainer teaches that "[formoterol] suspensions are preferred as they have proved particularly stable on storage" (col. 1, lines 66-67). In contrast, the present application requires that the formoterol be in solution. Moreover, Applicants note that the compositions containing formoterol in solution and steroidal anti-inflammatory in suspension as recited in claim 1 are surprisingly and unexpectedly stable. Typically, formulations having one drug in solution and one drug in suspension are not stable. Thus, in order to obtain a stable formulation, usually both drugs are provided either in suspension or in solution. Even Hochrainer teaches that the formoterol can be in solution or suspension, but does not disclose formulations having one drug in solution and another in suspension. In contrast, the present application provides that the formoterol is in solution and the steroidal anti-inflammatory is in suspension. In fact, claim 1 expressly recites that the formoterol is in solution and the steroidal anti-inflammatory is in suspension. Therefore, the stability of the claimed compositions having formoterol in solution and a steroidal anti-inflammatory in suspension is unexpected. Thus, Hochrainer actually teaches away from compositions of the present application, and the claims of the present invention are not obvious. *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1740 (2007) (stating that "when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious").

In addition, Hochrainer does not teach or suggest compositions wherein the formoterol concentration is about 5 μg/mL to about 200 μg/mL. The Examiner states that Hochrainer teaches "a known bronchodilator, particularly stable on storage with concentration 10-500 mg/ml" (Examiner's emphasis). The compositions suitable for long term storage in Hochrainer have a formoterol concentration of from 10 mg/mL to 500 mg/mL. However, this range is 2000-100,000 times greater than the lower limit and 50-2500 times greater than the upper limit of the formoterol concentration claimed in the present application. The lowest range taught by Hochrainer for administration is 0.9 mg/mL to 1.5 mg/mL (col. 4, lines 26-28). However, this range is 180-300 times greater

than the lower limit and almost 5-8 times greater than upper limit of the formoterol concentration claimed in the present application. The lowest concentration of formoterol taught in Hochrainer is 900 μg/mL (col. 4, lines 27-28). Thus, the lower limit of the claimed range of the formoterol concentration is 180 times more dilute than the lowest concentration taught in Hochrainer. The upper limit of the claimed range of the formoterol concentration is nearly 5 times more dilute than the lowest concentration taught in Hochrainer. Moreover, the compositions of Hochrainer having a formoterol concentration of 900 μg/mL are for administration, not for long term storage (col. 3, line 66-col. 4, line 28). Thus, again, Hochrainer teaches away from the present invention because Hochrainer teaches that compositions containing 900 μg/mL would not be stable for long term storage. Therefore, contrary to the Examiner's position, Hochrainer teaches that the claimed compositions are not predictable. *KSR*, 127 S. Ct. at 1740 (teaching away from combining certain known elements supports a finding of nonobviousness).

The Examiner recognized that Hochrainer does not teach compositions with steroid in suspension in propellant-free water, and cited Carling, PDR, Hardman, Leckie and Remington's Pharmaceutical Services to teach those elements. Applicants respectfully submit that these secondary references do not cure the deficiencies of Hochrainer, and thus, would not lead one of skill in the art to the present invention.

Although Carling teaches the combination of formoterol and steroid, Carling does not teach compositions containing dilute concentrations of formoterol, and steroid in propellant-free water, where the formoterol in solution and steroidal anti-inflammatory in suspension. Moreover, Carling does not teach compositions that are stable for long term storage and suitable for direct administration without dilution. To infer that such would have been obvious or even obvious to try would be impermissible hindsight. *KSR* should not be relied upon by the Examiner. This is not a case where "there are a finite number of identified, predictable solutions." *KSR*, 127 S. Ct. at 1727. On the contrary, the Examiner has provided no evidence in the prior art, or elsewhere, that the claimed subject matter would have been obvious. Thus, Carling does not cure the deficiencies of Hochrainer.

The Examiner cited the PDR to teach the use of steroids for treating asthma. Although the PDR teaches that steroids are useful in the treatment of asthma, the PDR

does not teach pharmaceutical compositions comprising dilute concentrations of formoterol in solution and steroid in suspension, in propellant-free water, which is suitable for long term storage and direct administration. Thus, the PDR does not cure the deficiencies of Hochrainer and Carling.

Moreover, the teachings of Hardman, Leckie and Remington's Pharmaceutical Sciences do not cure the deficiencies of Hochrainer, Carling and the PDR. Hardman, Leckie and Remington's Pharmaceutical Sciences do not disclose compositions with formoterol and steroid in propellant-free water that are suitable for long-term storage and direct administration without dilution. Thus, the secondary references in combination with Hochrainer, Carling and the PDR neither teach nor suggest the pharmaceutical compositions of the present invention.

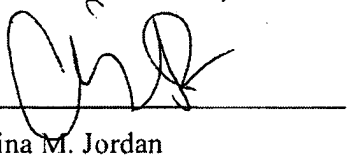
Since none of the references cited by the Examiner in combination with Hochrainer teach or suggest dilute aqueous solutions containing a combination of formoterol and steroid, where the formoterol is in solution and the steroid is in suspension, in propellant-free water, and where the dilute aqueous solutions are suitable for both long term storage and direct administration, it is respectfully submitted that the combination of the references cited by the Examiner would not have led one of ordinary skill in the art to the claimed invention. Thus, applicants submit that the claims presented herein are patentable over the Examiner's rejections and that this application is in condition for allowance and such action is respectfully and earnestly requested.

F. **FEES**

This response is being filed within the shortened period for response, thus no further fees are believed to be due. If it is determined that any further fees are due or any overpayment has been made, the Assistant Commissioner is hereby authorized to debit or credit such sum to Deposit Account No. 02-2275. Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

Respectfully submitted,

LUCAS & MERCANTI, LLP



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